Page 51, Abstract

Applicant requests replacing the previously submitted abstract with the abstract on the next page.

FRAMEWORK-PATCHED IMMUNOGLOBULINS

ABSTRACT OF THE INVENTION

Framework (FR)-patching is a novel approach to modify immunoglobulin for reducing potential immunogenicity without significant alterations in specificity and affinity. Unlike previous described methods of humanization, which graft CDRs from a donor onto the frameworks of a single acceptor immunoglobulin, we patch segments of framework (FR1, FR2, FR3 and FR4), or FRs, to replace the corresponding FRs of the parent immunoglobulin. Free assortment of these FRs from different immunoglobulins and from different species can be mixed and matched into forming the final immunoglobulin chain. A set of criteria in the choice of these FRs to minimize or eliminate the need to reintroduce framework amino acids from the parent immunoglobulin for patching is described. The approach gives greater flexibility in the choice of framework sequences, minimizes the need to include parent framework amino acids, and, most importantly, reduces the chances of creating new T- and B-cell epitopes in the resultant immunoglobulin.